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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/615,571	07/13/00	HARRIS	P 5951.010.US

025907
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EXAMINER	
DRABIK,C	
ART UNIT	**PAPER NUMBER**
1633	5

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/615,571	Applicant(s) HARRIS ET AL.	
	Examiner Christopher Drabik	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 51-70 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 51-70 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

Detailed Action

Claim 60 is objected to because of the following informalities: The identity of the claimed strain is unclear. Pg 51 appears to disclose that the name of the strain is E.coli pPH6. Appropriate correction is required such as amending claim 60 to read :"...contained in E Coli pPH6 as deposited with NRRL under accession number B-30142."

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 61 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 61 is drawn to an isolated nucleic acid **produced** by hybridizing an unspecified DNA under low stringency conditions to a second DNA of specified sequence. It is not possible to synthesize or make a nucleic acid solely by hybridization. Proper wording of the claim might be : "A nucleic acid isolated by (a) hybridizing a DNA under low stringency conditions..."

Claim 66 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 66 recites the limitation "the host cell" in claim 65. There is insufficient antecedent basis for this limitation in the claim.

Claims 67-70 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 67 recites a nucleic acid construct comprising a nucleic acid sequence and a gene encoding a protein. Said gene is foreign to the nucleic acid sequence. The term foreign does not adequately define the metes and bounds of the claim because the term foreign does not provide enough information to determine the scope of the claim. It is not defined what "foreign" means in relation to the nucleic acid sequence.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51, 52, 54, 56, 58, 59, 61-66 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1117. The specification does not "clearly allow persons of

ordinary skill in the art to recognize that [he or she] invented what is claimed."Vas-Cath Inc. v. Mahurkar, 19USPQ2d at 1116.

While the specification provides adequate written description for the claimed invention with regard to the Aspergillus oryzae phospholipase B nucleic acid sequence, the specification fails to describe the other species within the genus of nucleic acid sequences encoding proteins having phopholipase B activity encompassed in the claims with particularity to indicate that applicants had possession of the claimed invention. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). In the instant case, the claimed embodiment of any and all phospholipase B encoding sequences isolated from any and all microorganisms other than those specifically described for in Aspergillus oryzae, lack a written description. The specification fails to describe in sufficient detail the essential elements of the phospholipase B sequences present in microorganisms other than Aspergillus oryzae.

The skilled artisan cannot envision the detailed chemical structure of all of the encompassed nucleic acid sequences as claimed encoding phospholipase B activity isolated from any and all microorganisms, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Although the applicants describe the sequence of only one phopholipase B

gene, the claim encompasses any and all sequences having only 65% amino acid identity or 65 % nucleic acid homology which have phospholipase B activity. Applicants have only provided evidence for the possession of the nucleic acid of SEQ ID NO 1 and the amino acid sequence for SEQ ID NO 2. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the sequence for A. oryzae. Therefore, only the phospholipase B encoding nucleic acid isolated from A.oryzae meets the written description provision of 35 U.S.C. §112, first paragraph.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 51-56,58,59, 61-66 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acids specified as SEQ ID NO 2 encoding a polypeptide having phospholipase or the nucleic acid having the sequence encoding the polypeptide of SEQ ID NO 1, is not enabling for 1.) isolating nucleic acid sequences coding for a polypeptide having phospholipase B activity wherein the nucleic acid has only 65 % homolgy to nucleotides 568 to 2045 of SEQ ID NO 2, 2.) isolating nucleic acid sequences coding for polypeptides having

phospholipase activity wherein the nucleic acid codes for a polypeptide having 65 % homology to amino acids 20 to 646 of SEQ ID #2 or 3.) isolating sequences with phospholipase B activity hybridizing under low stringency conditions to nucleic acid sequences anticipated by SEQ ID NO 2, 4.)identifying allelic variants of any phospholipase B gene hybridizing under low stringency conditions to nucleic acid sequences of SEQ ID 1, 5)identifying allelic variants of any phospholipase B gene hybridizing under low stringency conditions to the nucleic acid sequences anticipated by the polypeptide of SED ID NO2, 6.) identifying nucleic acid subsequences encoding polypeptides having phospholipase B activity The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claim 51 is drawn to an isolated nucleic acid comprising either 1.) nucleotides 568 –2045 of SEQ ID 1 or 2.) the nucleic acids sequences predicted to encode the amino acids 20 – 464 of SEQ ID NO 2. Said isolated nucleic acid includes sequences having 65% identity to SEQ ID NO 1 or nucleic acid sequences encoding proteins which have 65% identity to the polypeptide of SEQ ID NO 2. Said isolated nucleic acid also includes nucleic acid sequences which hybridize under low stringency conditions with nucleotides 568 to 2045 of SEQ ID NO 1, hybridize under low stringency conditions to complementary sequences of nucleotides 568 to 2045 of SEQ ID NO 1, hybridize under low stringency conditions to subsequences of nucleotides 568 to 2045 of SEQ ID NO 1 or complementary strands thereof. Said isolated nucleic acid can comprise allelic variants of the aforementioned nucleic acids. Said isolated nucleic acid also

encompasses subsequences of aforementioned nucleic acid sequences with phospholipase B activity. Claims 52- 60 and 62-64 depend from claim 51 and hence are bound by the limitations of claim 51. Claim 61 falls within the same limitations as claim 51 with the rejoinder of reciting isolating the isolated nucleic acid.

While applicants clearly describe the sequence of the nucleic acid encoding phospholipase B from Aspergillus oryzae, the claims read on an enormous number of potential sequences. The apparent intended use of the disclosed sequence IDs is for the prospective identification of phospholipase B genes in other organisms. Indeed, the preferred embodiment most relevant to the rejected claims reads: "The nucleic acid sequences of SEQ ID NO1 or a subsequence thereof, as well as the amino acid sequence of SEQ ID NO 2 or a fragment thereof, may be used to design a nucleic acid probe to identify and clone DNA encoding polypeptides having phospholipase B activity from strains of different genera or species according to methods well known in the art." (page 5 lines 15-18). Critical to the use of the invention commensurate with the claims is the ability to identify genes with phospholipase B activity.

In reviewing the current state of the art regarding the cloning of cognate genes, Agnan et al write that many hurdles often not mentioned in the literature may be encountered when screening DNA libraries using a heterologous gene as a probe. (Agnan et al (1997) Fungal Genetics and Biology 21: 292-301; page 392, 2nd col para 2-3). Weak hybridization signals between probe and heterologous genomic DNA can be problematic. "The DNA probe can hybridize with different affinities to genomic DNA from different, but related organisms. A weak hybridization signal , however, will present a

major hurdle in cloning of the cognate gene, not only because it is difficult to detect , but also because it is difficult to differentiate signal from non-specific hybridization." (Agnan et al pg 294, 2nd col, 3rd full para). They further suggest that the ideal probe contain the complete gene segment as the DNA probe. It should be noted that applicants claim nucleic acids comprising only a fraction of the phospholipase B gene. It can be concluded from Agnan et al that using a nucleic acid of a known sequence to search for similar genes in different organisms is incompletely predictable even when the gene sequences are nearly homologous.

Given the potentially enormous number of sequences claimed, applicants have not provided a means for predictably identifying sequences which have 65% homology or identity to the disclosed SEQ IDs which also have phospholipase B activity. In addition applicants have not provided the design of even one hybridization probe capable of identifying a nucleic acid sequence having phospholipase activity under any sort of hybridization condition. While it is not argued that one skilled in the art could make probes based on the sequences provided, the ability to use every sequence encompassed by the claims to isolate nucleic acids having phospholipase B activity is not taught by the applicant.

Claim 65 and 66 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the production of a polypeptide using techniques well known in the art of protein expression and purification, does not reasonably provide enablement for the expression and purification of said polypeptide in all strains of

microorganisms. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 65 is drawn to the production of a polypeptide having phospholipase activity in a strain of microorganism under conditions suitable for the production of said polypeptide. Claim 66 depends from claim 65 and is also drawn to the production of polypeptides having phospholipase B activity The art of protein expression using recombinant vectors and purification of proteins thereof is well established for a limited set of microorganisms, for example E.coli or yeast. However, the breadth of the claim encompasses the production of said polypeptide in any strain of microorganism given suitable conditions. While it is not argued that the production of said protein could be accomplished using methodologies well established in the art, the ability to express and/or recover the protein from any and all strains of microorganisms is unpredictable. The applicants do not provide what they deem as suitable conditions for producing a polypeptide having phospholipase B activity in any and all strains of microorganisms, therefore the invention can only be enabled for strains of microorganisms established in the art at the time of filing. In addition, it is not apparent that, even if in a given microorganism the gene were transcribed and a protein translated, the recovery of said polypeptide would be easily accomplished by one skilled in the art. Given that direction for the recovery of said polypeptide from any and all forms of microorganism is also not provided, the recovery of said protein is limited in enablement to microorganisms and purification methodologies well known in the art at the time of filing.

Conclusions

Claims 57 and 60 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 51- 56, 58,59, and 61-70 stand rejected for the reasons set forth above.

Claims 51-70 are free of prior art of record based on the finding that nucleotide sequence 510-567 operabley linked to a gene encoding a protein has not been previously disclosed.

No claims are currently allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher Drabik whose telephone number is 703-605-1156. The examiner can normally be reached on Monday-Friday from 9am to 5pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on 703- 305-4051. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Inquiries of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-

1234. Questions regarding review of formality issues may be directed to Kim Davis, the patent analyst assisting in this application. She may be reached at 703-305-3015.

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